No. 31015/43/2017-Pricing
GOVERNMENT OF INDIA
MINISTRY OF CHEMICALS & FERTILIZERS
DEPARTMENT OF PHARMACEUTICALS
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A- Wing, Shastri Bhawan,
New Delhi 110 001

Subject: **Review application of M/s Mylan Pharmaceuticals Private Limited against price fixation of "Amphotericin B Powder for Injection - Lipid Liposomal" vide NPPA order No. S.O. 788(E), dated 10.03.2017 issued under Drugs (Prices Control) Order, 2013 (DPCO 2013).**

Ref: **1) Review application dated 06.04.2017**
2) NPPA notification under review S.O. 788(E), dated 10.03.2017
3) Record Note of discussions held in the personal hearing held in the matter on 30.05.2017.

1. This is a petition under paragraph 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) filed by M/s Mylan Pharmaceuticals Private Limited (hereinafter called the petitioner) against notification S.O. No.788(E), dated 10.03.2017 issued by the National Pharmaceutical Pricing Authority (hereinafter called the NPPA) fixing the ceiling price of Amphotericin B Powder for Injection - Lipid Liposomal.

2. The petitioner has contended as under:-

I. It is to be noted that by the said Notification, prices of brands belonging to separate and dissimilar drug delivery formulations viz., (a) "Liposomal Amphotericin B" ("L-Amb") small unilamellar/multilamellar liposomes with mean diameters <100 nm which is a novel drug delivery formulation, (b) Amphotericin B Lipid Complex (ABLC) a large molecule (1600-11000 nm) with a ribbon-like structure and inferior than liposomal Amphotericin B and (c) "Amphotericin B Lipid Emulsion ("ABLE") which is not a liposomal preparation but merely an Oil in water emulsion of Amphotericin B, with no specialized lipid drug delivery system or any incremental value, have been compared and a single ceiling price has been fixed. Such comparison amongst dissimilar formulations is unjust and unfair and against the mandate of the DPCO 2013 itself.

II. The Applicant is aggrieved by the said Notification inter-alia, on account of the following reasons:

(i) Price of products of Amphotericin B viz L-Amb (Applicant's AmBisome) formulation which is a novel drug delivery formulation, ABLC which has inferior safety profile (when compared to L-Amb) and ABLE (Amphomul) which has neither any specialized drug delivery system nor any incremental innovation, have been compared for the purpose of fixation of a single ceiling price.

(ii) The prices of products whose manufacturing licenses have been directed to be suspended by the Central Government have been taken into consideration.

(iii) The NPPA has failed to realize that the ceiling price revision by the said Notification ought to have been under Paragraph 18 (ii) of the DPCO 2013 and market data of August 2015 could not have been taken into account for such revision.

(iv) Abbott has wrongly been mentioned as the company name for AmBisome. AmBisome is the product of the Applicant.

(v) The per unit Price to Retailer (PTR) of AmBisome has been wrongly mentioned. The per unit price of Ambisome is Rs. 3869.10, the price that has been taken into account is Rs. 4040.

(vi) Amphomul and Amfy have been considered twice; and

(vii) Prices of formulations which are below 1% SKU wise MAT have been factored in calculation.

III. Company further submitted that to reduce the toxicity of Amphotericin B and increase its therapeutic index, three Non-conventional lipid formulations were separately developed through rigorous procedure of process development and testing, viz. (a) ABLC, (b) L-Amb and (c) ABCD. It is to be noted that various lipid based formulations were being developed (including lipid based emulsion) however, only three formulations were successful in obtaining FDA approval.

IV. **L-Amb AmBisome is an innovator product and cannot be compared with Amphomul, which is an ABLE product as both are separate formulations**. The sophisticated manufacturing process of the AmBisome liposomes, results in better quality, efficacy and safety compared to other lipid preparations including lipid emulsion (viz. Amphomul).

(i) The product stability in vivo, the tissue distribution, and the level of drug entrapment in the liposome particle are established not only by the product composition but by the manufacturing process and associated quality checks. **There are clear cases of very different quality in formulas that are ostensibly identical. As such, grouping AmBisome (a Liposomal technology product) with Amphomul (an oil in water emulsion product) for the purpose of pricing is unreasonable and arbitrary**. Such grouping inter-alia, ignores the processes required to manufacture Ambisome, an antifungal agent with molecular characteristics that establish it as unique antifungal properties.

(ii) Importantly, AmBisome has been approved by multiple global agencies for a host of indications after a large number of clinical trials. Amphomul, on the other hand, has been approved for only 2 indications, and the clinical trials done for Amphomul are very small in size.

(iii) Similarly **Liposomal Amphotericin B (L-Amb) a bioengineered nanoparticle of size less than 100 nm with negative charge and liposomal delivery system cannot be compared to ABLC. ABLC is a large molecule (1600-11000 nm) with a ribbon-like structure. Because of its large size, it is taken up rapidly by macrophages resulting in rapid clearance from the bloodstream. In contrary LAmB because of its small size and negative charge, avoids substantial recognition and uptake by the mononuclear phagocyte system and therefore has a prolonged circulation time.**

ABLC has an inferior safety profile when compared to Liposomal Amphotericin B. L-Amb has a superior safety profile in comparison with ABLC, along with better tolerance, significantly fewer infusion-associated reactions, and significantly lower nephrotoxicity.

V. In 2013, the ceiling price of "Amphotericin B Injection" of strength 50 mg/vial pack was notified by the NPPA at **Rs. 4,245.32** per pack vide notification number S.O. 1912(E) dated 28th June 2013.

(i) The aforementioned notification was challenged by two companies, viz. Lifecare Innovations Private Limited and Panacea Biotech under paragraph 31 of the DPCO 2013 before this Reviewing Authority, by applications dated 10.7.2013 and 23.08.2013 respectively. The companies sought review of the said notification on the ground inter-alia, that the data used by the NPPA to arrive at the ceiling price of Amphotericin B included both liposomal as well as lipid formulations of Amphotericin B, even though liposomal and lipid formulations are different products. It was also asserted inter-alia, that clubbing dissimilar products was not in the interest of industry and research and ultimately the patient.

(ii) During the same period, the Applicant and its partner Gilead Sciences Inc. also submitted representations to NPPA seeking an opportunity to present their case regarding the grouping of AmBisome with other alternative formulations of Amphotericin B.

(iii) During the pendency of the abovementioned review applications and representations, the ceiling price of "Amphotericin B" injection was revised by the NPPA to **Rs. 4513.62** per pack as per annual revision vide notification number S.O. 1156(E) dated 28.04.2014.

(iv) In the same year, i.e. in 2014, the Director General of Health Services, Government of India, being concerned on account of reports related to safety and efficacy of the generic version of liposomal Amphotericin B available in the market, issued a letter to fourteen (14) manufacturers of Liposomal Amphotericin B informing them that the Department of Health and Family Welfare had constituted a Committee to examine the quality, safety and efficacy of the drug Amphotericin B and requesting them to submit their comments.

(v) Thereafter, **by two separate orders in 2015, this Reviewing Authority disposed of the review applications filed by Lifecare Innovations Private Limited and Panacea Biotech while observing that the said applicants had a genuine case and recommended that the matter deserved consideration**.

Company has also attached the copies of the above said orders at **Annexure H** and **Annexure I of their application**.

VI. Meanwhile, in the year 2015, the ceiling price of Amphotericin B Injection was again revised to **Rs. 4687.35** per pack by notification No. S.O.619(E) dated 26.02.2015 issued by the NPPA.

In November 2015, the Core Committee for Revision of NLEM ("Core Committee") submitted its report on the criteria for inclusion and deletion of medicines in the NLEM. The Core Committee recommended inter-alia, that innovation in medicine must be encouraged and that formulations developed through incremental innovation/ novel drug delivery systems like inter-alia, lipid/liposomal formulations, should be considered differently for purposes such as procurement policy, pricing etc.

VII. In the year 2016, the ceiling price of "Amphotericin B" Injection was again revised to **Rs. 4560.30** per pack by notification No. S.O. 644(E) dated 02.03.2016 issued by the NPPA.

VIII. The **revised NLEM incorporated the recommendations of the Core Committee and created a distinction between "Amphotericin B (Conventional)" and "Lipid Liposomal Amphotericin B" and included them as separate classes under Entry No. 6.3.1 for "Amphotericin B". Even while revising the NLEM in 2015, it was not considered that "Lipid Liposomal Amphotericin B" was not a single class but were grouped under it separate drug delivery formulations deserving separate treatment. It was further ignored that there were separate and distinct drug delivery systems where L-Amb(Ambisome) is a true liposomal specialised novel drug delivery system and ABLE on the other hand is neither a Liposomal preparation nor a specialised lipid drug delivery system with any incremental innovation but an oil in water emulsion with minimal clinical studies and approvals.**

IX. Company further submitted that after the said revision of the First Schedule of the DPCO 2013, even though the NPPA was under a mandate under paragraph 17 of the DPCO 2013, to fix the ceiling price of the newly added entry "Lipid Liposomal Amphotericin B" under paragraph 18 (i) of the DPCO 2013 within 60 days of such addition or revision of First Schedule (until 10.05.2016), the same was not done.

X. In March 2016, the Central Government advised the State Licensing Authorities to suspend the manufacturing licenses of liposomal Amphotericin B of ten manufacturers in public interest as they could not prove the safety and efficacy of their products. Company has also attached the copies of Lok Sabha Questions and newspaper on the above said matter at **Annexure K and Annexure L of their application**.

XI. Thereafter, the said Notification was passed on 10.03.2017 {(S.O. 788(E)}, fixing the ceiling price of "Amphotericin B Powder for Injection - Lipid Liposomal" at **Rs. 3,328.61** per pack on the basis of market data of August 2015.

XII. Being aggrieved by such fixation of ceiling price, the Applicant is therefore constrained to file the present Review Application, inter alia, on the following grounds which are without prejudice to each other:

A. **L-Amb (a bioengineered liposomal technology), ABLC and ABLE (A Lipid emulsion) are different Drug Delivery Formulations and the price of brands thereof cannot be compared for the purpose of fixation of ceiling price:**

A.1. The lipid compositions of L-Amb, ABLC and ABLE formulations differ considerably. Whereas Ambisome (L-Amb) is a true liposomal drug delivery system, ABLC and Amphomul are not liposomal preparation. Amphomul is not a specialized lipid drug delivery system with an incremental innovation. The manufacturing processes involved in L-Amb are more robust, complex, carefully controlled, precise and quality controlled in comparison to Amphomul which is a preparation of Amphotericin B suspended in an oil-in-water emulsion base which does not require any robust manufacturing capabilities. ABLC is a large molecule and has an inferior safety profile when compared to Liposomal Amphotericin B.

A.2. **The DPCO mandates comparison of different brands of the same formulation and does not require that cost of brands of separate formulations should be compared for price regulation. The NPPA has however clubbed and compared the price of products belonging to separate and dissimilar drug delivery formulations** viz.,

(a) "Liposomal Amphotericin B" ("L-Amb") comprising of small unilamellar / multilamellar liposomes with mean diameters <100 nm which is a novel drug delivery formulation;

(b) Amphotericin B Lipid Complex (ABLC) a large molecule (1600-11000 nm) with a ribbon-like structure and inferior than liposomal Amphotericin B; and

(c) "Amphotericin B Lipid Emulsion ("ABLE") which is not a liposomal preparation but merely an Oil in water emulsion of Amphotericin B, with no specialized lipid drug delivery system or any incremental value.

A.3. On account of such grouping/clubbing, under the Said Notification, the price of the Applicant's product AmBisome (a nanotechnology based liposomal product), belonging to the L-Amb category, has been compared with the price of dissimilar ABLE product (Amphomul) (a conventional formulation of Amphotericin B in an oil and water mixture), and ABLC product (Ampholip and Amphotin lip) and a single ceiling price has been fixed;

A.4. That such clubbing of two distinct and separate novel drug delivery system formulations under the same class has led to unfair and unjust comparison of unlike products for price fixation;

A.5. That such clubbing of Liposomal formulation, which is distinct and separate having a novel drug delivery system, along with a formulation which is neither distinct nor is a novel drug delivery system or any incremental innovation, under the same

class is repugnant to the very intent of revision of the National List of Essential Medicines 2011, which is to incentivize innovation in medicine.

A.6. Such unfair price fixation which discounts the fact that the cost of production of different formulations vary and cannot be compared, has made it commercially unviable for the Petitioner to continue to make AmBisome available in India at the notified ceiling price.

A.7. **Company also submitted that the current clubbing is also wrong in view of Paragraph 11 (3) and (4) of the DPCO, 2013.**

B. **Comparison with suspended formulations:**

B.1 The NPPA has **compared the price of the Applicant's product AmBisome, with the price of products, the manufacturing licenses of which had been directed to be suspended by the Central Government on account of serious concerns regarding their safety, efficacy and standard**. Fixation of ceiling price by comparing the price of a quality product with products whose safety, efficacy and quality are circumspect and which are not even in the market at the time of fixation of such ceiling price is unfair, unjust and wholly arbitrary.

C. **The Ceiling price of the subject formulation ought to have been fixed under paragraph 18 (ii) of the DPCO 2013, on account of suspension of certain products under advise of the Central Government and consequent change in the market structure.**

C.1. The DPCO 2013, clearly provides that when the number of manufacturers of a scheduled formulation, having price of a scheduled formulation more than or equal to seventy-five percent of the ceiling price fixed and notified by the Government, has decreased by twenty-five percent or more than the number of manufacturers as existing on the last date of revision of ceiling price, the ceiling price ought to be revised under paragraph 18 (ii).

C.2. As the manufacturing licenses of a large number of brands selling liposomal Amphotericin B had been directed to be suspended by the Central Government, the NPPA at the first instance, ought to have enquired whether the market structure had changed substantially so as to warrant a revision under paragraph 18 (ii). Such enquiry would have revealed that the market structure of the subject Liposomal Amphotericin B products had changed since the last revision and therefore the revision ought to have been under paragraph 18 (ii).

D. **Market Data of August 2015 could not have been considered for the purpose of fixing ceiling price of the subject schedule formulation in March 2017**.

D.1. The DPCO 2013 nowhere provides that in order to calculate the revised ceiling price under paragraph 18 (ii), market data of two years prior to such revision ought to be used. It is submitted that the NPPA was bound to collect current data while revising ceiling price in March 2017. Use of market data of the period prior to

the change in market structure would defeat the very purpose of such revision under paragraph 18 (ii).

D.2. Paragraph 9(5) is applicable for a revision of ceiling price under paragraphs 17 and 18(i) i.e. when there has been a revision of the First Schedule to the DPCO 2013. The provisions of paragraph 9 (5) which allows the use of market data of six months prior to the notification of revision in the First Schedule could not have been applied for the current revision of ceiling price.

D.3. The NPPA was under a mandate under paragraphs 17 and 18 (i) of the DPCO 2013 to fix the ceiling price of the subject schedule formulation within sixty dates of notification of the revision of the First Schedule whereby such formulation was added, i.e. on or before until May 10, 2016. Upon failure to do so, it could not have treated the revision in the current years as a revision under paragraphs 17 and 18 (i) and used the market data of August 2015.

E. **Glaring errors in the calculation of ceiling price by the Said Notification:**

E.1. An examination of the working sheet published by the NPPA (Annexure A) discloses inter-alia, the following glaring infirmities in fixation of the ceiling price for "Lipid Liposomal Amphotericin B":

(a) Market data for August 2015 has been considered despite there having been a substantial change in the market structure since July 2016;

(b) Abbott has wrongly been mentioned as the company name for AmBisome. AmBisome is the product of the Applicant.

(c) The per unit price (PTR) of AmBisome has been wrongly mentioned. The per unit price of Ambisome in August 2015 was Rs. 3869.10, the price that has been taken into account is Rs. 4040.

(d) Price of Amphomul, which is an ABLE (Oil in water emulsion of Amphotericin B), has been compared with inter-alia, AmBisome which is an L-Amb i.e. a Bioengineered Liposomal technology product, even though both are dissimilar and unlike formulations whose prices differ considerably;

(e) Price of suspended products which were not in the market in August 2016, has been compared with the price of the AmBisome, i.e. the Applicant's product;

(f) Amphomul and Amfy have been considered twice; and

(g) Prices of formulations which are below 1% SKU wise MAT have been factored in calculation.

XIII. **In view of the above mentioned facts and circumstances, company prayed that**:

(a) The ceiling price fixed for 'Lipid Liposomal Amphotericin B' by the said Notification, being **Notification No. S.O. 788 (E) dated 10.03.2017** be

reviewed with immediate effect and Liposomal Amphotericin B (L-AmB), Amphotericin B Lipid Complex (ABLC) and Amphotericin B Lipid Emulsion brands be considered separately under Schedule I for the purpose of fixation of ceiling price.

(b) An Expert Committee may also be appointed, under the DPCO, 2013 (including paragraph 11 of DPCO, 2013), to examine the current common classification of L-AmB drug delivery formulation, amphotericin B lipid complex (ABLC) and Emulsion products which are neither incremental innovations nor novel drug delivery formulations.

(c) This Authority may consider fixing / revising the ceiling price of Liposomal Amphotericin B products separately under paragraph 19 in public interest.

3. **Comments of NPPA:**

Company has stated that correct methodology was not followed in arriving at the ceiling price for **Amphotericin B 50mg Powder for Injection- Lipid/Liposomal**. The points raised by the company are not relevant. Price fixation has been done strictly in accordance with the provisions of DPCO, 2013.

PART A (FACTS)

Without prejudice it is submitted

1. THAT a case of similar nature has been filed by M/s Lifecare innovations Ltd. in respect of Amphotericin B Injection 50mg.
2. THAT M/s Gilead Inc., USA being manufacturer having permanent place of business in India at in India at Level 3, Neo Vikram, New Link Road, Andheri West, Mumbai, 400058 India. (source : http://www.gilead.com/about/worldwide-operations/asia/india)
3. THAT M/s Gilead Sciences Ireland UC having office at IDA Business & Technology Park, Carrigtohill, Country Cork, Munster is the manufacturer as per Annexure B (Form 41) of review application and has not filed Form V, Form II, and Form III for at-least last five years in respect of this Formulation which is required under the DPCO 2013.
4. THAT Ministry of Commerce called a meeting on dated under the chairman of Shri Ali R Rizvi, Joint Secretary, Department of Commerce on 26.5.2017 to discuss the Request for an Expedited Review of a price Control for Amphotericin B Powder for Injection – Lipid/Liposomal. The meeting was represented by M/s GSI Pharma Pvt Ltd (a subsidiary/associate of Gilead Inc), M/s Gilead Inc, M/s Mylan Pharmaceuticals jointly represent their case. The official from NPPA and CDSCO were also present.
5. THAT M/s Mylan Pharmaceuticals Pvt Ltd. has not filed the Form V, Form II, FORM III in respect of this subject matter " AMBISOME" for the period 2013-2014, 2014-15,2015-16. The filing prior to 2013-14 is yet to be verified. The non-filing of the forms/returns by the M/s Mylan Pharmaceuticals Ltd. lead to delay in examining the matter and finalise the matter.

PART B (Parawise Comments)

Details are as follows:**-**

Sl. No.	Company's Grievances	NPPA's comments
1.	Company has stated that NPPA has considered the PTR of Liposomal Amphotericin B alongwith the PTR of Amphotericin B Lipid complex formulation to derive the ceiling price for **Amphotericin B 50mg Powder for Injection-Lipid/Liposomal.**	In this regard it is stated that Amphotericin B:- (a) Amphotericin B (Conventional) (b) Lipid / Liposomal Amphotericin B are included in section 6.3.1 and section 6.5.2 of **NLEM 2015** by Ministry of Health & Family Welfare and included in Schedule – I (Amended vide S.O. 701(E) dated 10.3.2016) of DPCO 2013 by DoP. NLEM 2015 **does not differentiate between Liposomal Amphotericin B and Lipid formulation of Amphotericin B**, therefore, NPPA has rightly fixed the ceiling price Rs. 275.62 / pack for Amphotericin B Powder for Injection – Conventional and Rs. 3328.61/pack for Amphotericin B Powder for Injection – Lipid/Liposomal vide S.O. 788(E) dated 10.3.2017, which has been revised to Rs. 281.05/pack and Rs. 3394.25/pack respectively vide S.O. 1039(E) dated 01.4.2017 considering the WPI increase impact. Further, DPCO 2013 clearly states the averaging of prices of formulation considering the formulation as one group. The sub-categorisation of the same formulation on the basis of the prices is not a principle of price control as per NPPP 2012. By sub-classifying on the prices, the highly priced product will remain high, thus do not confirm with the objective of the policy. Further, the classification of the formulation exists in every formulation of the DPCO 2013. In this regard, NLEM Recommendations (page 34) states "*The Committee decided that in general, medicines should be mentioned in the NLEM in terms of their active moieties, without mentioning the salts. However, in case, where, the different salts of a medicine have significant difference in potency/ pharmacokinetics/ pharmacodynamics/ efficacy safety profile, the medicine has been mentioned in the list with respect to its specific salt. The Committee also considered that in case a medicine is available in more than one salt without any significant difference in above aspects, it is implied that all salts of that medicine with specified dosage form and strength are considered included in NLEM, 2015.For example, diclofenac is available as*

		diclofenac sodium or diclofenac potassium. However there is no significant difference in the above mentioned aspects, between the two salts. Hence only diclofenac is mentioned in the NLEM, which implies that both diclofenac sodium and diclofenac potassium are included in the NLEM" In respect of subject formulations Lipid and Liposomal has been mentioned as single line Item. Hence, for pricing purpose, it is considered same. The NLEM 2015 committee recommendations (page 36) states "*Consideration of representations* *The Core-Committee received more than 50 representations from institutions, industry associations, pharmaceutical companies, NGOs, as well as individual experts. The committee considered these representations. Wherever considered appropriate, the viewpoints have been included in the NLEM.* *Conclusion* *Revision of NLEM has been a complex process in the light of fast changing concepts in medicines, treatment regimens, introduction of new technologies and incremental innovations in drug delivery systems and formulations, wide differences in medical practice pattern in the country, regional variations in health care system etc. Further dimension has been added because of measures of Government to regulate prices of all medicines included in NLEM which has increased the importance of process of revision of NLEM."* In the light of statement of the NELM committee, it is understood that the case of Amphotericin B Lipid/Liposomal has been already examined by the NLEM Core Committee and Committee after due consideration has included the medicines has mention Lipid/Liposomal as one formulation for the purpose of essentiality and pricing. To put more light, M/s Gilead Inc / M/s Mylan may state that whether they have submitted any representation to Core Committee of NLEM.
2.	Company has stated that Liposomal Amphotericin B is a novel drug delivery formulation as compare to Amphotericin B Lipid	In the light of explanation above, it is stated that Liposomal form as well as Lipid have same drug(formulation) being Amphotericin B. The Pharmaceutical pricing policy considers the formulation as unit for averaging. The sub-class of

	complex formulation.	formulations exists in every formulation. For Pricing, the drug mentioned in schedule I or NLEM 2015 is taken as one.
3.	Company has clarified above the marketing agreement with M/s Gilead Sciences Inc.	The contents of the petitioner seem to be incorrect. The Annexure B of the review application states agreement with Gilead Sciences Ireland UC which is different from Gilead Sciences Inc. The applicant may submit the copy of such agreement for clarity of the issue.
4.	Point – 4, (i)- Company has repeated the same issue as point out in S. No. 1.	The common ceiling price has been given for the lipid/Liposomal Injection as per the predefined procedure under DPCO 2013. The common ceiling price donot means that these products are considered same. The prices are to be fixed the manufacturer, the government has fixed the ceiling price only. Within the ceiling prices the competition plays an important role.
	Point - 4(ii) and (iii) Licenses suspended	Suspension of the Licenses is routine process of CDSCO. The data was taken from Pharmatrac and the said SKU were available in the market as of Aug 2015 MAT. Even the import License of M/s Mylan was granted on 4-Aug-2016 as per Annexure B of the application. There is no provision in the DPCO to do adjustment of such suspension. Hence, the data was considered as per DPCO 2013 provisions. However , the NPPA do-not have confirmation of suspension/discontinuation.
5.	4. (iv to v) – Company has pointed out that AmBisome is their product and does not belong to M/s Abbott as shown in calculation sheet. Actual PTR of AmBisome is Rs. 3869.10 against Rs. 4040.	DOP vide letter no. F. No. 31015/44/2016-PI.I dated 11.7.2016 gave the following, directions: "*NPPA to henceforth place a draft version of the Price Calculation Sheets for the proposed revised price notification, including wherever applicable, the Price to Retailer (PTR) and Moving Annual Turnover (MAT) values adopted for calculations, on the website of NPPA for 10 clear working days to invite comments from the affected pharmaceuticals firms. Only after taking into account the comments or any additional data thus received within the given time period, the NPPA shall finalize the Ceiling and the Retail Prices. This issues with the approval of Hon'ble Minister (Chemicals & Fertilizers)*". Accordingly, NPPA uploaded draft working sheet of proposed ceiling price of this formulation also on its website. This was on the website of NPPA for 10 clear working days. **M/s Mylan Pharmaceuticals Pvt. Ltd. <u>did not make</u> any representation against the proposed draft ceiling price uploaded on NPPA's website**. When the draft was uploaded on 17-Feb-2017.

		Further , the manufacturer vide letter OM dated 7.2.2017 was also required to submit copies of sample invoice to retailer, sample, summary of all invoices as per, copies of IPDMS submission. Further, where the representation is made on the basis of discontinuation of any brand/packsize the burden of proving this contention 'with verifiable documentary evidence' lies with the pharmaceuticals company. The applicant company has not submitted any application at the after uploading of draft. These documents are even not submitted during the review application process. The applicant should have such facts, which has the effect to reduce the ceiling price.
6.	Point – 4, (vi) – Amphomul and Amfy of M/s Bharat Serums & M/s Intas Pharmaceuticals Ltd. has been considered twice.	The applicant has not raised any objection, however, the statement of fact is noted.
7.	Point – 4, (vii) – Prices of formulations which are below 1% SKU wise MAT have been considered in calculation.	The name mentioned in the Brand column are basically the trademark not brands (this is reported as brand by Pharmatrac) . The definition of the brand para 2(c) of DPCO 2013 emphasis on seller i.e Company. In true sence, NPPA has followed the DoP order.
8.	Point - 5 - Company has stated that subject formulation is for treatment of Kala Azaar and invasive fungal infections.	Not relevance with DPCO provisions.
9.	Point - 6 to 10 – Company has also stated that to reduce the Toxicity and increase the efficacy of Amphotericin B three non-conventional have been developed and approved by FDA from time to time. L-Amb AmBisome liposomes have the better quality, efficacy and safety as compared to other lipid preparations including lipid emulsion.	All are the variants of Amphotericin Lipid formulation. Issues raised by company have no relevance with DPCO provisions.

10.	Point – 11 to 13 – Company has pointed out that Liposomal Amphotericin B (L-Amb) is a bioengineered nanoparticle of size less than 100nm with negative charge and Liposomal delivery system cannot be compared to ABLC which is a large molecule (1600 – 11000nm).	Better quality of Liposomal Amphotericin B (L-Amb) has no relevance with the provisions of DPCO, 2013 unless it is specified separately in NLEM 2015.
11.	Point – 14 to 30 – Related to history of regulatory changes in price control of Amphotericin B.	In respect of para 16, The matter shall be examined. In respect of Para 27, it is to state the NPPA vide its OM dated 13.5.2017 has uploaded on the website that the PTR, MAT data relates to Amphotericin B 50 mg Lipid/Liposomal is not available and ask the companies to submit the data. The said OM was followed by the series of OM. The Last OM in respect of Amphotericin B was uploaded on 10.1.2017 but the applicant did not provide the relevant information of the PTR/MAT. The intention of the applicant is mischievous in this respect. All other content of these para are not relevant in DPCO 2013.
12.	Points against prayer.	In respect of the application under para 19 of the DPCO 2013.The product is being imported at USD 30 per vial. i.e around Rs. 2060 per injection.

PART C (other Facts)

14. The further classification of Lipid anf Liposomal will be anti-competitive. In another application by M/s Mylan Pharmaceuticals Ltd. with CCI (para 28 & 17 of case no 68 of 2016) , the co-applicant of M/s Mylan has prayed the investigate into the alleged anti-competitive practices and abusive conduct adopted by the Roche Group. its affiliates, group entities, distributors (including Emcure) and agents. Besides, through a separate interim relief application dated 28th July, 2016, the Informants have, inter-alia, prayed that the Roche Group should be restrained from approaching doctors, regulatory authorities, officials of State and private tender committees and making any representation on the medicinal reputation of CANMAb and HERTRAZ produced and marketed by the Informants. The facts of case are similar to this case.

15. Company has not challenged any notification in respect of **Amphotericin B 50mg Powder for Injection- Lipid/Liposomal** in the Court. However, another applicant has challenged in the court.

4. Examination:

The petitioner company stated that NPPA has erred in price fixation of their formulation **Amphotericin B Powder for Injection - Lipid Liposomal** on the ground that NPPA has considered the PTR of Liposomal Amphotericin B alongwith the PTR of Amphotericin B Lipid complex formulation to derive the ceiling price for **Amphotericin B 50mg Powder for Injection- Lipid/Liposomal.** According to Company, Liposomal Amphotericin B is a novel drug delivery formulation as compare to Amphotericin B Lipid complex formulation. In this connection, it is stated that as per Schedule I, conventional formulation is shown as a separate category and lipid/liposomal as a separate category. NLEM 2015 does not differentiate between Lipsomal Amphotericin B and Lipid formulation of Amphotericin B. It is also understood that the case of Amphotericin B Lipid/Liposomal has already been examined by the NLEM Core Committee and Committee after due consideration has included the medicines Lipid/Liposomal as one formulation for the purpose of essentiality and pricing. In view of this, NPPA has rightly considered the PTR of Liposomal Amphotericin B along with the PTR of Amphotericin B Lipid complex formulation to derive the ceiling price for **Amphotericin B 50mg Powder for Injection- Lipid/Liposomal.** Therefore, the grievance of the petitioner has got no merit and cannot be considered.

As regards the other grievance of the petitioner company that Abbott has wrongly been mentioned as the company name for AmBisome, which is their product and the per unit price (PTR) of AmBisome has been wrongly mentioned and also the per unit price of Ambisome in August 2015 was Rs.3869.10, whereas the price that has been taken into account is Rs.4040, NPPA may be directed to examine the information/documents submitted by the petitioner company on merit.

The company also stated in its petition that prices of formulations which are below 1% SKU wise MAT have been factored in calculation. On examination, it is found that NPPA has erred in calculating ceiling price as per para 4 of DPCO, 2013. The DPCO does not recognise a company for average PTR but only medicines/ formulations. Thus, only those formulations are to be considered, which are having MAT value of more than 1% market share. On going through the calculation sheet, it is observed that the number of formulations which are to be considered having more than 1% market share and number of formulations to be excluded, as per table given below:-

Formulation name	**Number of brands to be considered having more than 1% market share**	**Number of brands to be excluded**
Amphotericin B Powder for Injection - Lipid Liposomal	8	3

In view of the above, the hearing authority is of the opinion that NPPA may be directed to refix the ceiling prices of the formulations by considering only those medicines / formulations having MAT value of more than 1% market share, as DPCO does not recognise a company for average PTR but only medicines / formulations.

5. **Government Decision:**

"Schedule I of NLEM 2015 does not differentiate between Lipsomal Amphotericin B and Lipid formulation of Amphotericin B. As per Schedule I, conventional formulation is shown as a separate category and lipid/liposomal as a separate category. NPPA has rightly considered the PTR of Liposomal Amphotericin B along with the PTR of Amphotericin B Lipid complex formulation to derive the ceiling price for Amphotericin B 50mg Powder for Injection- Lipid/Liposomal. Therefore, the grievance of the petitioner has got no merit and cannot be considered."

"NPPA is also directed to examine the information/documents furnished by the petitioner company about the formulation AmBisome being their product and the actual PTR of the formulation and make necessary correction, on merit."

"NPPA is further directed to refix the ceiling prices of the formulation Amphotericin B Powder for Injection - Lipid Liposomal by considering only those medicines / formulations having MAT value of more than 1% market share, as DPCO does not recognise a company for average PTR but only medicines / formulations."

Issued on this date, the 7th day of September,2017.

(M.K. Bhardwaj)
Deputy Secretary
For and on behalf of the President of India

To

1. M/s. Mylan Pharmaceuticals Private Limited,
   No.32/1 & 34/1 to 4, 7th to 12th Floor,
   Prestige Platina, Block 3, Kadubesanahalli Village,
   Varthur Hobli, Outer Ring Road, Bangalore East Taluk,
   Bengaluru-560 087.
2. The Member Secretary,
   National Pharmaceutical Pricing Authority,
   YMCA Cultural Centre Building, New Delhi-110001

Copy to :

1. PS to Hon'ble Minister (C&F), Shastri Bhawan, New Delhi for information.
2. PSO to Secretary (Pharma), Shastri Bhawan, New Delhi for information.
3. T.D., NIC for uploading the order on Department's Website